* 1. Tissue types affected by sarcomas, carcinomas, and hematopietic and lymphoid tumors
  + **sarcomas:** tumor in mesenchymal tissues
    - bone, muscle Connective tissue, or neural tissue
  + **carcinomas**: tumor in epithelia tissue
    - cells lining intestines, bronchi and mammary glands
  + **hematopoietic and lymphoid**: spread through the bone marrow, lymphatic system and peripheral blood
    - leukemia and lymphoma
* 2. Describe the two major types of familial colon cancer, the genes affected and the mechanisms leading to cancer formation.
  + Colorectal cancer-15% of cancer in US
  + Two types
    - **Familial Adenomatous polyposis (FAP)**
      * 1% of colon ca
      * mutation in adenomatous polyposis coli(APC) gene
      * heterozygotes have lots of adenomatus polyps which are originally benign but 1 or more usually become malignant
      * tx: colectomy- remove colon
      * \* if you have this mutation you have >95% chance of getting colon cancer
    - **Hereditary Nonpolyposis Colon Cancer (HNPCC)**
      * 2-4% of colon ca
      * mutation in **MSH2 & MLH1** genes- (normal fxn is to carryout mismatch repair [MMR] of genes)
      * there are 5 known MMR genes that carry mutations for HNPCC
      * if you have the mutation you have a 60-80% chance you will get colon cancer
* 3. list common cellular roles of proto-oncogenes
  + promote cell growth and survival
  + encode transcription factors
  + inhibit apoptosis
  + signal cell proliferation
* 4.states the difference between gatekeeper and care taker tumor suppressor genes
  + gatekeeper genes: control cell growth, block tumor growth by cell cycle regulation and help mediate apoptosis
  + caretaker genes: protect the integrity of the genome, a loss of function of caretakers allows mutations to occur
    - encode:
      * proteins for detecting and repairing mutations
      * proteins involved in normal chromosome disjunction during mitosis
      * components of programmed cell death machinery
        + most common caretaker gene affected: **p53- it is mutated in 50% of tumor cells**
* 5. Events that convert prot-oncogenes to oncogenes
  + point mutations
    - Ras
      * First oncogene isolated
      * Encodes a GTP binding protein
        + G-proteins = ‘on/off’ switch on when Ras bound, off when Ras not bound
        + Activates or inactivates downstream molecules controlling transcription and translation
      * Activated Ras is always on (always bound to GTP) which casuses increase of growth and proliferation pathways
  + Deletion mutations
    - Remove regulatory domain
      * RTK’s
  + Chromosome translocations
    - Produce novel fusion proteins
      * Bcr-Abl
    - Juxtapose a stronger promoter upstream causes the proto-oncogene to not be expressed properly
      * Bcl2 (follicular lymphoma)
  + Gene amplifications
    - Causes overexpression
      * TF: N-Myc
      * RTK: Her2 in breast cancer
* 6. Explain p53’s role in neoplasia
  + - helps regulate the cell cycle by detecting and repairing DNA damage
    - **\*MUTATED in 50% of human tumors**
    - somatic mutations very common in:osteosarcomas, breast, colon, pancreatic, and solid tumors
    - most mutations are MISSENSE that interfere with functional domains
    - mutations allow cancer cells to proliferate in presence of DNA damage or oncogene stress
    - myc over expression can cause apoptosis in wt p53 expressing cells
    - Constituational mutation
      * Ass w/ Li fraumeni cancer predisposition syndrome
        + Autosomal dominant inheritance
        + Penetrance is increased more for women than men
        + High breast ca risk

Av age: 32

Multiple malignancies

New mut cases common as well

* 7. Define:
  + Neoplasia
    - Uncontrolled cell proliferation causes a mass/tumor (neoplasm)
  + Malignant tumor
    - Cancer- has uncontrolled cell growth capable of metastasizing
  + Benign tumor
    - Can be cancerous/noncancerous.
    - Not capable of metastasizing
  + Sarcoma
    - Tumor in mesenchymal tissues
      * Bone, muscle, connective tissue or neural tissues
  + Carcinoma
    - Tumor in epithelial tissues
      * Cells lining intestines, bronchi, mammary glands
  + Hereditary cancer: inherited through the germline
  + Sporadic cancer: due to a somatic mutation,
  + Oncogenes mutations: dominant effect at the cellular level ie. When activated/overexpressed a single mutant allele is enough to initiate the change in phenotype of the cell from normal to malignant
  + Tumor suppressor genes TSG’s
    - Mutations are recessive at the cellular level, ie effect is only seen when wt allele is lost by mitiotic or epigenetic silencey
      * Gatekeeper TSG’s
        + Control cell growth, and block tumor growth by cell cycle regulation
        + In control of cell cycle check points
        + Mediate apoptosis

Ex: RBI

Encodes for P110, -cell cycle control. Mutated in retinoblastoma (familial) and small cell carcinomas along with breast cancer (sporadically)

TP53

Encodes for p53-cell cycle control. Ass w/ LI-fraumei syndrome(familial) and lung&breast ca. (sporadically)

VHL

Encodes for vhl-inhibits blood vessel growth when oxygen present. Ass w/ von hippel-linudau syndrome(familial) & clear cell renal carcinoma (sportatically)

* + - * Caretaker TSG’s
        + Protect the integrity of the genome
        + When loss of function (LOF) of caretakers it allows mutations to accumulate

BRAC1/BRAC2

Responsible for chromosome repair for double stranded DNA breaks

Encodes proteins responsible for responding to DNA damage and Phosphorylation by ATM protein

Common mut in familial breast cancer

Mutations common throughout and are deleterious ie either frameshifts or nonsense mutations

\*does not follow the 2-hit hypothesis

only if you inherit the BRAC-1 mutation does it increase your cancer risk

LOH is common in tumors of BRAC1 carries

No somatic mutations in BRAC1

Lifetime risks

Breast cancer: 50-80%

Ovarian cancer:15-40%

Men w mut allele have slight increased risk of male breast ca and an increased risk of prostate cancer

MLH1/MSH2

See above

* + Loss of hertozygosity (LOH)
    - Caused by mitotic recombination. Lose on of your alleles, and if you lose the wt allele you now are only expressing the mutant allele and will begin expressing the pheontype